Case Report

Congenital Malignant Rhabdoid Tumor of the Skin

-Report of A Case and Review of the Literature

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Malignant rhabdoid tumor is a well-established clinicopathologic entity occurring classically in the kidney and central nervous system in children. Cutaneous origin has rarely been reported. We herein report a male newborn infant presented with an erythematous and ulcerated mass on his lower back at birth and was found to be a malignant rhabdoid tumor, diagnosed by histopathologic and immunohistochemical studies. In spite of aggressive treatment with chemotherapy and surgery, cerebral and pulmonary metastases developed later. The patient finally died at 10 months of age. This rare case is reported and literatures are reviewed. (Dermatol Sinica 27: 227-234, 2009)

Key words: Malignant rhabdoid tumor, Skin

INTRODUCTION

Malignant rhabdoid tumor (MRT) was originally defined as a distinctive neoplasm which developed in the infant kidney. 1 Since 1982, many cases of MRT arising from extrarenal sites including brain,2,3 liver,4 heart,5 pelvis,6 soft tissue of neck, extremities, abdominal, chest wall,7,8 and rarely skin9,10 have been reported.11 Akin to the rhabdoid tumors originally described in kidney, extrarenal rhabdoid tumors also display a uniformly aggressive clinical course and were found predominantly in childhood and infancy. Histologically, the tumor is characterized by cellular proliferation of poorly differentiated neoplastic cells with large and eccentric nuclei, prominent nucleoli and eosinophilic cytoplasm. We report a primary cutaneous rhabdoid tumor in a neonate and also review the literature. To our knowledge, this is the eighth reported case of primary cutaneous rhabdoid tumor.

CASE REPORT

A full-term male infant was born to a gravida 1, para 1 mother via vaginal delivery. At birth, an erythematous and polypoid nodule with ulceration measuring 3 x 3.5 cm presented on his lower back (Fig. 1). An excisional biopsy was performed under the impression of an undifferentiated sarcoma. Pathological study on hematoxylin and eosin sections showed hyperkeratosis and eosinophilic infiltrates of tumor cells in dermis (Fig. 2A)
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The tumor cells had large round nuclei and small nucleoli with appreciable amount of eosinophilic cytoplasm (Fig. 2B, 2C). They formed interlacing fascicles with moderate mitotic activity. Immunohistochemical study showed that the tumor cells were positive for vimentin (Fig. 3A), epithelial membrane antigen (EMA) (Fig. 3B), cytokeratin (AE1/AE3) (Fig. 3C), smooth muscle actin, neuron specific enolase (NSE), chromogranin A and S-100 protein. They were negative for desmin, HHF-35, CD34, CD68 and factor XIIIa. Given the results of the studies and the lack of definite muscle, neural or melanocytic differentiation, a diagnosis of MRT was made. Computed tomographic (CT) scan was arranged for tumor workup and disclosed residual tumor in the skin with involvement of subcutaneous fat tissue. No involvement of brain, chest, abdomen and pelvis was found.

The patient underwent surgical wide resection of the tumor. Postoperative course was uneventful. Two months after surgery, the child was readmitted due to projectile vomiting caused by increased intracranial pressure. Magnetic resonance imaging of the brain showed a fourth ventricle tumor with obstructive hydrocephalus. Surgical intervention of the brain tumor was performed. The tumor was found to be a metastatic MRT (Fig. 4). Multiple lung nodules were also detected by whole body CT scan. They
were believed to be pulmonary metastases of the same tumor. He was then treated with two courses of chemotherapy with ifosfamide, carboplatin, and etoposide. The patient died of multiorgan failure at 10 months of age, about 2 months after initiation of chemotherapy.

**DISCUSSION**

MRT was first described in 1978 by Beckwith and Palmer as a variant of nephroblastoms (Wilms tumor). It was called “rhabdoid” originally to imply rhabdomyosarcoma-like features, now the rhabdoid features are known to be cytoplasmic globoid aggregates of keratin and vimentin intermediate filaments. Since then, a number of reports have documented the occurrence of similar lesions in a variety of extrarenal sites. Cutaneous MRT, either primary or metastatic is rare. Reviewing the English language literature, our case is the eighth case of primary cutaneous malignant rhabdoid tumor (Table 1). The 8 patients including the present case consisted of 5 females and 3 males. Including our patient, there are 3 congenital cases. The other two were infants and three were adults. The tumors of neonates and infants were located in the back and shoulder. Two of three adult cases occurred in the leg. The tumors might clinically resemble as hemangioma. All the cases of cutaneous MRT developed metastasis months later. The average survival time was 10 months after diagnosis in cases whose data were available (Table 1). Sajedi M et al. reviewed 21 patients with extrarenal noncentral nervous system congenital MRT from 1983 until 1999.

| Table. 1 Primary Cutaneous Rhabdoid Tumor in the English-Language Literature |
|-------------------------------|----------------|----------------|----------------|-------------------|----------------|
| Case | Age/Sex | Tumor site | Therapy | Metastasis | Outcome/follow-up (months) | Author (year)ref |
| 2 | 42 year/M | Right leg | S | N.A. | N.A. | Sangueza OP et al., (1992) |
| 3 | 14 month/M | Back | S | Brain | Dead (5) | Boscanio A et al., (1994) |
| 4 | 1 day/M | Shoulder | S | Widespread metastases | Dead (3) | Perez-Atayde et al., (1994) |
| 5 | 1 day/F | Shoulder | S/CT | Lung | Dead (29) | Albrechts AE et al., (1996) |
| 6 | 3 month/F | Upper scapula | S | Widespread metastases | Dead (9) | Grañon-Bustinduy et al., (1999) |
| 7 | 53 year/F | Right leg | S/CT | Lung, adrenal glands, iliac bones | Dead (8) | Pettit M et al., (2005) |
| 8 | 1 day/M | Back | S/CT | Lung, brain | Dead (10) | Present case |

S: surgery, CT: chemotherapy
N.A.: not available
diagnosed within the first month of birth. 90% of patients (19 patients) had disseminated disease at onset. For those cases with disseminated disease at presentation, soft tissue of the trunk, head and extremities were the most commonly reported primary location. Lung and liver were the most common sites of metastasis, followed by lymph nodes. Instead of having disseminated involvement at onset like most congenital extrarenal noncentral nervous system MRT cases, congenital primary cutaneous rhabdoid tumor developed metastasis months later.13, 14

Immunohistochemical staining shows marked heterogeneity. The most common and constant profile is the coexpression of vimentin and epithelial markers including cytokeratin and epithelial membrane antigen (EMA). Neural or neuroectodermal makers such as CD99, synaptophysin are also frequently expressed in MRT. The expression of muscle specific actin and focal S-100 protein expression is not an uncommon feature, but diffuse immunopositivity for S-100 protein has not been reported. Desmin, myoglobin and CD34 are usually not expressed in tumor cells. The apparent phenotypic heterogeneity has created some controversy with regard to the origin of these tumors. Many different lines of cellular differentiation have been proposed, including mesenchymal, myogenous, epithelial, histiocytic and neuroectodermal.13

Cytogenic and molecular analyses has shown that deletion of the long arm of chromosome 22 (22q 11, 2) is a recurrent genetic characteristics of MRT. This finding has led to the identification of hsNF5/INI1/SMARCB1/BAF47 as a candidate tumor-suppressor gene involved in the pathogenesis of renal and extra-renal rhabdoid tumor.23, 24 Because of these IN1 gene alterations, immunohistochemical loss of IN1 protein has been observed in MRT and positive nuclear staining is preserved in other non-rhabdoid tumor cells.27 Therefore, recent studies have found that immunohistochemical study for IN1 antibody aided in confirming the histological diagnosis of renal or extra-renal rhabdoid tumors. Besides, mutations of P53 tumor suppressor gene was found in renal and extra-
renal rhabdoid tumor. The alterations of P53 gene may have an important role to play in the aggressive biological behavior of MRT.

The histological differential diagnosis includes other tumors with rhabdoid features such as epithelioid sarcoma (ES), rhabdomyosarcoma, and rhabdoid malignant melanoma. An extensive battery of immunohistochemical stains are needed to exclude other tumors. Classical distal-type ES, which usually affects the distal extremities, may have focal areas resembling rhabdoid tumor. However, the numbers of rhabdoid cells are small and they are focally recognized. Histologically, in ES, tumor cells tend to form nodular aggregates with central necrosis. Therefore, it may be easily differentiated from MRT. On the other hand, proximal-type ES, which more frequently affects the pelvis and perineum, usually present more rhabdoid cells and lacks the typical “granuloma-like” appearance as classical type and make the differential diagnosis difficult. However, the peak age for the incidence of proximal-type ES is early adulthood and adolescence; cases in patients under the age of 10 years are rare. Furthermore, its clinical course is less aggressive than MRT. Comparing the expression of adhesion molecules between MRT and proximal-type ES immunohistochemically, CD34 is frequently positive in ES but negative in extrarenal rhabdoid tumor. Besides, β-catenin expression was reported to be aided in distinguish ES from MRT. None of the MRT cases had expression of β-catenin, whereas two out of three proximal-type ES cases had membranous expression. The clinicopathological, immunohistochemical distinction between MRT and ES are summarized in Table 2.

Rhabdomyosarcoma with extensive rhabomyoblastic differentiation may look morphologically similar to rhabdoid tumor, but diffuse positivity for myoid markers, including desmin and myoglobin, will support the diagnosis. Rhabdoid malignant melanoma can be distinguished from rhabdoid tumor by diffuse positive S100 protein staining since only focal S100 protein is occasionally found in rhabdoid tumor.

Most cases of MRT, regardless of its primary site, have poor prognosis. The presence of metastasis at diagnosis seems to be the only prognostic factor of outcome. Multimodal therapy with surgery, chemotherapy, and radiation therapy has been recommend-
ed. But complete remission is uncommon. In the review study of the 21 patients with congenital extrarenal, non-central nervous system MRT, the median survival time was 2.0 months. The median survival time for these patients who received chemotherapy as part of their treatment was significantly longer than for those who did not receive chemotherapy. Although the survival is statistically longer than those who didn’t receive chemotherapy, it was not clinically relevant because all patients died within months of diagnosis. Allogeneic hematopoietic stem cell transplantation was performed after surgery and multiagent chemotherapy in one case of congenital disseminated MRT. But the patient only remained in clinical remission for 3 months and died 12 months after pulmonary metastases.

In summary, primary cutaneous MRT is a rare malignant tumor. Although MRT occurs mostly in infancy and early childhood, congenital occurrence is very rare. MRT in an uncommon location is easily misdiagnosed as other types of tumor. Thus the diagnosis should be made by thorough histologic and immunohistochemical studies. This case is reported to emphasize the importance of considering the possibility of MRT in a neonate with skin tumor.

REFERENCES
先天性皮膚惡性類橫紋肌肉瘤
- 病例報告及文獻回顧

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惡性類橫紋肌肉瘤 (Malignant Rhabdoid Tumor) 是一種典型好發在小孩腎臟及中樞神經系統，不論在臨床及病理學上都已有共識的腫瘤。然而，發生在皮膚上卻是非常罕見。我們報告一位男嬰，出生在下背部發現一個紅色、表面潰瘍的皮膚腫塊。經皮膚切片以及免疫組織化學診斷為類橫紋肌肉瘤。儘管病人接受了積極的外科手術及化學治療，腫瘤之後轉移到肺部及腦部。最後他在10個月大時死亡。我們在此提出一個皮膚惡性類橫紋肌肉瘤的病例報告以及文獻回顧。（中華皮誌: 27: 227-234, 2009）